REMARKS/ARGUMENTS

In response to the Office Action mailed February 4, 2010, Applicant amends his application and requests reconsideration. Claims 1-28 were originally pending in this application. Claims 10-28 are withdrawn as directed to a non-elected invention. Claims 1-9 are pending and undergoing examination.

Claims 1, 4, 5-6, and 9, have been amended to further clarify and refine that which Applicant considers to be the invention. These amendments correct minor errors of form or grammar, and are fully supported in the specification as filed. No new matter has been added by these amendments.

Discussion of the Claim Rejections under 35 U.S.C. §112, second paragraph

The Examiner rejected claims 1, 4, 5-6, and 9, under 35 U.S.C. §112, second paragraph, as being indefinite. In view of Applicant's amendments to the claims, Applicant submits this rejection is rendered moot. Applicant therefore respectfully requests withdrawal of this rejection.

Discussion of the Claim Rejections under 35 U.S.C. §103(a)

The Examiner rejected claims 1-6 under 35 U.S.C. §103(a), as obvious over Liu et al. (Biomed. Microdevices, 4:257-266 (2002)), in view of Subramanian (Seminars in Neurology, 21:103-115 (2001). According to the Examiner, Liu et al. allegedly teach a biodegradable, photopolymerizable polymer gel that can be used with certain cell types to deliver cells to patients. The Examiner also alleges that Subramanian teaches that human retinal pigmented epithelial cells (hRPE) can be implanted into patients to treat Parkinson's disease. Thus, the Examiner alleges that one of ordinary skill in the art, at the time the invention was made, would have been motivated to combine the teachings of Liu et al. with Subramanian, to arrive at Applicant's claimed invention. Applicant respectfully disagrees.

For subject matter defined by a claim to be considered obvious, the Office must demonstrate that the differences between the claimed subject matter and the prior art "are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said

subject matter pertains." 35 U.S.C. § 103(a); see also *Graham v. John Deere Co.*, 383 US 1, 148 USPQ 459 (1966). The ultimate determination of whether an invention is or is not obvious is based on certain factual inquiries including: (1) the scope and content of the prior art; (2) the level of ordinary skill in the prior art; (3) the differences between the claimed invention and the prior art, and (4), objective evidence of nonobviousness. *Graham*, 383 US at 17-18, 148 USPQ at 467.

Applicant respectfully submits that while Liu et al. teach photopolymerizable hydrogels for use in osteografts and other tissue replacement therapies (not cellular) and wound care devices, they do not teach the use of these materials for transplantation of neuronal cells into the brain, nor do they teach or suggest that such materials could be adapted for this use. Moreover, there is no teaching in Liu et al., that the crosslinked PEGDMA polymer used is actually biodegradable. As the hydrogel construct is supposed to replace a tissue in the body, one of ordinary skill would expect that such a construct would not be designed to degrade over time, but rather, be permanent. Finally, the monomer used by Liu et al., is not recited in any of Applicant's claims or the specification. Claim 2 of Applicant's invention recites poly(ethylene glycol) di-[ethyl phosphatidyl (ethylene glycol) methacrylate], also known as "PhosPEG-dMA," a phosphate-containing and photocrosslinkable polymer.

The deficiencies of Liu et al. are not cured by the teachings of Subramanian. Subramanian teaches use of a different type of cells, fetal ventral mesencephalic (FVM) cells, which are not derived from the substantia nigra, or retina, as claimed by Applicant. In addition, on page 109, Subramanian teaches that RPE cells do not differentiate to make synaptic connections like FVM cells, and thus, teaches away from their use in treating Parkinson's disease.

Consideration of the aforementioned Graham factors here indicates that the present invention, as defined by the amended claims, is unobvious in view of specification and claims of the present patent application.

Considering all of the Graham factors together, it is clear that the Applicant's invention, as presently claimed, would not have been obvious to one of ordinary skill in the art, at the relevant time, in view of the prior art references. Furthermore, a rationale to support a conclusion that a claim would have been obvious requires that

all the claimed elements were known in the prior art and one skilled in the art could have combined the elements as claimed by known methods with no change in their respective functions, and the combination would have yielded nothing more than predictable results to one of ordinary skill in the art. *KSR International Co. v. Teleflex Inc.*, 550 US 398, 408, 82 USPQ2d 1385, 1395 (2007).

The Court in *KSR* noted that obviousness cannot be proven merely by showing the elements of a claimed device were known in the art; it must be shown that those of ordinary skill in the art would have had some "apparent reason" to combine the known elements in the fashion claimed. *KSR* at 1741. In the same way, when the prior art teaches away from the claimed invention, as shown in Appellant's arguments and other objective evidence, obviousness cannot be proven by merely showing that the biopolymer composition and growth factors were known, or that RPE cells could be modified by routine experimentation. See, *Ex parte Whalen* II, Appeal 2007-4423, (BPAI July 23, 2008) at pp. 13-16.

In contrast to the teachings of Liu et al. or Subramanian, Applicant's claimed invention provides an entirely different method for treating Parkinson's disease, by implanting cells from the substantia nigra, or RPE cells, into the brain for integration into the brain tissue. Applicant's invention is based on injection or implantation of a suspension of cells and photo-induced polymerization *in-situ* after implantation. This allows the cells to have sufficient support in the brain tissue, but only for a limited period of time, due to the degradation of the biopolymer substrate, leaving the implanted cells in the brain. The Examiner has provided no substantive reasoning as to why one of ordinary skill in the neurological disease art, would look to a reference which teaches photopatterning of hydrogels which are not biodegradable (Liu et al.) for use in preparing artificial tissues or organs, and attempt to combine that teaching with injection of cells into the brain (Subramanian) to treat Parkinson's disease, when the latter reference also teaches that Applicant's preferred choice of cells (RPE) would not likely be as successful for Applicant's claimed use.

In view of the foregoing, Applicant submits that the combination of teachings of Liu et al., in view of Subramanian, do not teach all the features of Applicant's claimed invention. Moreover, the Subramanian reference teaches away from the use of cells from the substantia nigra or RPE cells in the treatment of Parkinson's disease.

As such, the combination of teachings of Liu et al., in view of Subramanian, cannot render claims 1-6 *prima facie* obvious, and Applicant respectfully requests withdrawal of this rejection.

The Examiner also rejected claims 1-7 under 35 U.S.C. §103(a), as obvious over Liu et al., in view of Young et al., (International Patent Publication No. WO2003/018040). The teachings of Liu et al. were discussed previously. The Examiner offers Young et al., for allegedly teaching a composition comprising RPE cells, a biodegradable polymer, growth factors, and that the polymer could be a hydrogel. The Examiner argues that one of ordinary skill, at the time Applicant's invention was made, would have recognized that the strategies of Liu et al. could be employed with a reasonable expectation of success, in a composition comprising the cell types described by Young et al. The Examiner alleges that one of ordinary skill would have been motivated to do so, and would have had a reasonable expectation of success. Applicant respectfully disagrees.

Applicant has previously discussed the teachings of Liu et al. Young et al. teach a composite graft for the treatment of conditions associated with photoreceptor loss in the eye (AMD related blindness). The composite graft comprises a layer of connecting cells and a layer of photoreceptors. The connecting cell layer cells include, neural stem cells, such as retinal stem cells (RSC) or brain stem cells, or more differentiated neural progenitor types such as to give rise to bipolar cells in the retina, and RPE cells. According to Young et al., "sources of the different layers may be derived from healthy mammals, embryos, cadavers, or surgical specimens. An efficient method of obtaining the composite graft of the invention is to extract three layers of the graft from donor eyes-the RPE layer, Bruch's membrane and the photoreceptor layer-and then to lay down the connecting cell layer in cell culture." Young et al. also teaches that the Bruch's membrane can substituted temporarily by other biodegradable membranes (with or without added growth factors) such as Descemet's, amniotic or lens capsule, until the RPE makes a new Bruch's membrane. Young et al. also teach that RSC can be grown on a hydrogel and implanted in a retina.

It is clear that the teachings of Young et al. are directed to an entirely different disease, and its methods are directed to repair of the retina of the eye, not the subtantia

nigra of the brain of a patient suffering from Parkinson's disease. Applicant submits that the general teachings of Young et al. are inopposite to the general teachings of Applicant's invention. In Young et al, the authors are trying to put RPE back into the retina. In contrast, in Applicant's invention, Applicant is taking RPE out of the retina to implant into the brain to treat Parkinson's disease. Furthermore, while Young et al. does mention implantation of RPE, it is in the context of a graft containing other cells from the retina, which is excised out of a donor eye, not a cell suspension, as in Applicant's claimed invention. Furthermore, the only teachings in Young et al. regarding a hydrogel, is in combination with RSC cells for implantation into the subretinal space of the eye, and not, as in Applicant's invention, with RPE cells into the brain. Thus, Applicant submits that no one of ordinary skill in the treatment of Parkinson's disease, would have looked to the teachings of Young et al., nor would they have been motivated to do so, as the two areas of study and their modalities of treatment, are significantly different.

In view of the foregoing, Applicant submits that the combination of teachings of Liu et al., in view of Young et al., do not teach all the features of Applicant's claimed invention. Moreover, the Young et al. reference does not teach anything with regard to the treatment of Parkinson's or that RPE cells can be grown in biodegradable polymers for use in the treatment of Parkinson's disease. Moreover, one of ordinary skill in the treatment of Parkinson's disease would not have any reasonable expectation that the methods taught in Young et al., for treatment of AMD would be successful in treating Parkinson's disease. As such, the combination of teachings of Liu et al., in view of Young et al., cannot render claims 1-7 *prima facie* obvious, and Applicant respectfully requests withdrawal of this rejection.

The Examiner also rejected claims 1-8 under 35 U.S.C. §103(a), as obvious over Liu et al., in view of Young et al., and further in view of Calias et al. (U.S. Patent No. 6,749,865). The teachings of Liu et al. and Young et al. were discussed previously. The Examiner admits neither reference teaches the use of growth factors conjugated to polycarbophil. The Examiner offers Calias et al. for teaching that biopolymers can be conjugated to therapeutic agents, and that such agents are useful for drug delivery to specific cell types. The Examiner alleges that one of ordinary skill in the art would have been motivated to use a conjugate for specific targeting of

cell types, because the teachings of Liu et al., and Young et al. are directed to compositions comprising a cell-hydrogel matrix for tissue engineering, and would have a reasonable expectation of success in doing so. Applicant respectfully disagrees.

As stated with regard to the previous rejection, the combination of teachings of Liu et al., in view of Young et al., do not teach all the features of Applicant's claimed invention. Moreover, the Young et al. reference does not teach anything with regard to the treatment of Parkinson's disease, or that RPE cells can be grown in biodegradable polymers for use in the treatment of Parkinson's disease. Moreover, one of ordinary skill in the treatment of Parkinson's disease would not have any reasonable expectation that the methods taught in Young et al. for treatment of AMD would be successful in treating Parkinson's disease. The deficiencies of the combination of Liu et al. and Young et al. are not cured by the application of Calias et al. Calias et al. merely teach that therapeutic agents are capable of being covalently bound to biopolymers such as hyaluronic acid, or polycarbophil. Calias et al. do not teach or suggest treating Parkinson's disease by implanting cells from the substantia nigra, or RPE cells, into the brain for integration into the brain tissue. Nor does Calias et al. teach or suggest injection or implantation of a suspension of cells and photo-induced polymerization *in-situ* after implantation.

In view of the foregoing, and in view of Applicant's previous remarks with regard to Liu et al. and Young et al., Applicant submits that the combination of teachings of Liu et al., in view of Young et al., and further in view of Calias et al., do not teach all the features of Applicant's claimed invention. As such, the combination of teachings of Liu et al., in view of Young et al., and further in view of Calias et al., cannot render claims 1-8 *prima facie* obvious, and Applicant respectfully requests withdrawal of this rejection.

The Examiner also rejected claims 1-7, and 9 under 35 U.S.C. §103(a), as obvious over Liu et al., in view Young et al., and further in view of Frondoza et al. (U.S. Patent Application Publication No. 2001/00144575). The teachings of Liu et al. and Young et al. were discussed previously. The Examiner admits that neither reference teaches the use polyvinyl alcohols. The Examiner offers Frondoza et al. for teaching biodegradable polymers comprising polyethylene glycol and polyvinyl

alcohols, and that Frondoza et al. teach that implants made from these compositions can be crosslinked by photo-induction. The Examiner alleges that because the formulation methods of Liu et al. and Frondoza et al. are similar, one of ordinary skill in the art would have recognized that the biological matrices of Liu et al. could be modified, using the teachings of Frondoza et al., to incorporate the polyvinyl alcohol components as found in Applicant's claimed invention. The Examiner concludes that it would have been obvious, to one of ordinary skill in the art, at the time Applicant's invention was made, to combine the teachings of Liu et al., Young et al., and Frondoza et al. to arrive at Applicant's invention. Applicant respectfully disagrees.

As stated with regard to the previous rejection, the combination of teachings of Liu et al., in view of Young et al., do not teach all the features of Applicant's claimed invention. Moreover, the Young et al. reference does not teach anything with regard to the treatment of Parkinson's or that RPE cells can be grown in biodegradable polymers for use in the treatment of Parkinson's disease. Moreover, one of ordinary skill in the treatment of Parkinson's disease would not have any reasonable expectation that the methods taught in Young et al. for treatment of AMD would be successful in treating Parkinson's disease. The deficiencies of the combination of Liu et al. and Young et al. are not cured by the application of Frondoza et al.

Frondoza et al. teach a method of preparing cells for implantation comprising allowing cells (e.g., chondrocytes) to grow on microcarrier particles for an extended period of time and to secrete extracellular matrix components, thereby, producing a cell-microcarrier aggregate useful for implantation to a patient. The cell-microcarrier aggregates can be implanted directly or further cultured inside a mold that has been shaped to configure the geometry of the area of the body receiving the cells for implantation. When further cultured in a mold, cell-microcarrier aggregates are consolidated into an inplantable structure for repair or replacement of missing or diseased tissue. The microcarrier used to prepare the aggregate is a biocompatible, biodegradable material. There is no teaching or suggestion in Frondoza et al. about treatment of Parkinson's disease, or culturing of any cells from the substantia nigra or RPE cells. Furthermore, there is absolutely no teaching about the use of the microcarrier or aggregate of Frondoza et al. in the brain. The teachings of Frondoza

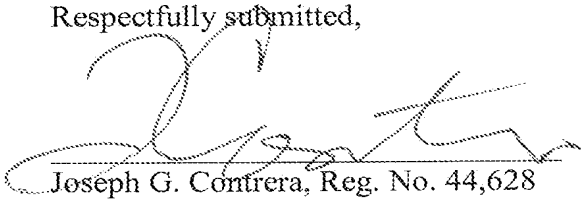
et al. are strictly limited to connective and soft tissue repair and the preparation of a resorbable matrix containing chondrocytes, which can be molded into certain body shapes.

In view of the foregoing, and in view of Applicant's previous remarks with regard to Liu et al. and Young et al., Applicant submits that the combination of teachings of Liu et al., in view of Young et al., and further in view of Frondoza et al., do not teach all the features of Applicant's claimed invention. As such, the combination of teachings of Liu et al., in view of Young et al., and further in view of Frondoza et al., cannot render claims 1-7, and 9, *prima facie* obvious, and Applicant respectfully requests withdrawal of this rejection.

Conclusion

Applicant respectfully submits that the patent application is in condition for allowance. If, in the opinion of the Examiner, a telephone conference would expedite the prosecution of the subject application, the Examiner is invited to call the undersigned attorney.

Respectfully submitted,



Joseph G. Contrera, Reg. No. 44,628
LEYDIG, VOIT & MAYER
700 Thirteenth Street, N.W., Suite 300
Washington, DC 20005-3960
(202) 737-6770 (telephone)
(202) 737-6776 (facsimile)

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